REMARKS

Pending Claims

Independent claims 40 and 50 have been amended. New claims 58 and 59 have been added. Claims 41-49 and 51-57 have been amended to depend from claims 58 and 59, respectively. Accordingly, claims 40-59 are pending. Claims 41-49 and 51-59 recite subject matter indicated allowable by the Examiner. No new matter has been entered by this amendment.

Allowable Claims

The Examiner has indicated claims 41-45 and 51-54 to be allowable in independent format. New claims 58 and 59 and dependent claims 41-49 and 51-57 recite this allowed subject matter.

Prior Art rejection

Claims 40 and 50 stand rejected under 35 U.S.C. §102(e), as being "inherently" 5,932,540 (Hu et al.) for reasons of record set forth in Paper No. 16, 7/27/2001. Under 35 U.S.C. §102(e), "a person shall be entitled to a patent, unless the invention was described in a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent". Applicants respectfully traverse this rejection.

The Examiner has not demonstrated the CIP's effective priority date.

The cited reference, Hu et al. USPN 5,932,540, was filed on December 24, 1997, citing two pending patent applications for priority: USSN 08/207550, 1994 and USSN 08/465,968, 1995. In order to claim the effective filing date of one or more of the parent priority applications, the subject matter claimed in the '540 CIP must reside in the parent priority disclosures. Neither patent application has issued as a U.S. Patent, however a divisional application of the 1994 USSN 08/207550, issued as USPN 5,935,820. The divisional patent demonstrates that the 1994 disclosure contained only a partial sequence of VEGF-2, lacking

amino acid residues 1 to 69. Accordingly, the sequence recited in the CIP is new matter in the Hu '540 patent, and is not entitled to the 1994 priority date.

Applicant is not aware of an issued US patent that demonstrates the full disclosure of the 1995 priority application, and respectfully requests that the Examiner provide evidience of description of the sequence disclosed in the 1995 patent application to demonstrate that priority can be properly claimed for this patent application.

The claimed method is not inherently disclosed by the cited reference.

The method claims under exaination in the pending case are not properly rejected under 35 USC 102(e) as inherently described in the Hu et al patent. Requirements for a rejection based on inherency are found, for example, in the Federal Circuit's holding in *In re Continental Can* (*Continental Can Co. v. Monsanto Co.)*, 948 F.2d 1264, 20 U.S.P.Q.2D (BNA) 1746 (Fed. Cir. 1991).

> An undisclosed element of the prior art **must** be a necessary technological fact of the prior art to find inherent anticipation, For a method claim to be inherently anticipated by a prior art reference, that prior art method must naturally produce a result or process that is claimed in the subsequent invention.

A published method may inherently anticipate a subsequently claimed invention when the method, as a natural consequence of its **structural** limitations, results in an outcome claimed by the later inventor. Moreover, the "inherent" characteristic of the prior art method must be **recognized** by those reasonably skilled in the art. *In re Leinoff* (*Leinoff v. Louis Milona & Sons, Inc.*, 726 F.2d 734, 220 U.S.P.Q. (BNA) 845 (Fed. Cir. 1984)), Leinoff claimed the result of a process that was already well known in the art, and thus was inherently anticipated. On the other hand, in *In re Rijckaert* (9 F.3d 1531, 28 U.S.P.Q.2d (BNA) 1955 (Fed. Cir. 1993)) Rijckaert's method disclosed more than the prior art, extending the art beyond what had been previously disclosed. Moreover, Rijckaert disclosed a relationship that was not recognized by those reasonably skilled in the art. These facts distinguished *Rijckaert* over *Leinoff.*

Applicants respectfully assert that the limitations of the instant claims are not met by the cited reference, explicitly or inherently. Like Rijckaert, the claimed method requires more than what is known in the prior art. For example, prior to the instant invention, the Flt4 receptor was

not associated in any way with VRP (VEGF2), and the discovery that this receptor binds VRP extends the knowledge of the prior art. Furthermore, the binding of VRP to Flt4 receptor and subsequent receptor phosphorylation would not have been recognized by those skilled in the art, as it is not a natural consequence of the teachings of the cited reference.

Accordingly, the cited reference Hu et al. does not teach or suggest the claimed invention. Removal of the inherency rejection is requested.

Conclusion

In light of the forgoing amendments and remarks, Applicants submit the claims are in condition for allowance. Early notice of allowance is requested.

The Examiner is invited to telephone the undersigned attorney for clarification of any of the amendments and remarks or to otherwise speed prosecution of this application.

Respectfully submitted,

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VERSION WITH MARKINGS TO SHOW CHANGES MADE

40. (Amended) A method for stimulating ~~the~~ tyrosine phosphorylation of a Flt4 tyrosine kinase receptor in a Flt4-expressing cell, comprising contacting the cell with a ~~composition comprising a~~ polypeptide comprising the amino acid residues 21-49 of SEQ ID NO:3 in an amount effective to stimulate ~~the~~ tyrosine phosphorylation of said Flt4 tyrosine kinase receptor.

41. (Amended) The method of claim ~~40~~ 58, wherein the polypeptide comprises ~~the~~ amino acid residues 1 to 49 of SEQ ID NO:3.

42. (Amended) The method of claim ~~40~~ 58, wherein the polypeptide comprises ~~the~~ amino acid residues 21 to 157 of SEQ ID NO:3.

43. (Amended) The method of claim ~~40~~ 58, wherein the polypeptide comprises ~~the~~ amino acid residues 1 to 157 of SEQ ID NO:3.

44. (Amended) The method of claim ~~40~~ 58, wherein the polypeptide comprises ~~the~~ amino acid residues 21 to 419 of SEQ ID NO:3.

45. (Amended) The method of claim ~~40~~ 58, wherein the polypeptide comprises the amino acid sequence of SEQ ID NO:3.

46. (Amended) The method of claim ~~40~~ 58, wherein the Flt4-expressing cell is *in vitro*.

47. (Amended) The method of claim ~~40~~ 58, wherein the Flt4-expressing cell is *in vivo*.

48. The method of claim 47, wherein the Flt4-expressing cell is an endothelial cell.

49. The method of claim 48, whercin the endothelial cell is in lymphatic endothelia.

50. (Amended) A method for promoting growth of endothelial cells that express ~~the~~ Flt4 tyrosine receptor, comprising contacting the cells with a polypeptide comprising:

~~the~~ amino acid residues 21 to 49 of SEQ ID NO:3,

in an amount effective to promote the growth of the endothelial cells.

51. (Amended) The method of claim ~~50~~ 59, wherein the polypeptide comprises ~~the~~ amino acid residues 1 to 49 of SEQ ID NO:3.

52. (Amended) The method of claim ~~50~~ 59, wherein the polypeptide comprises ~~the~~ amino acid residues 21 to 157 of SEQ ID NO:3.

53. (Amended) The method of claim ~~50~~ 59, wherein the polypeptide comprises ~~the~~ amino acid residues 1 to 157 of SEQ ID NO:3.

54. (Amended) The method of claim ~~50~~ 59, wherein the polypeptide comprises ~~the~~ amino acid residues 21 to 419 of SEQ ID NO:3.

55. (Amended) The method of claim ~~50~~ 59, wherein the polypeptide comprises the amino acid sequence of SEQ ID NO:3.

56. (Amended) The method of claim ~~50~~ 59, wherein the endothelial cells are *in vivo*.

57. The method of claim 56, wherein the endothelial cells are in lymphatic endothelia.

58. (New) A method for stimulating tyrosine phosphorylation of a Flt4 tyrosine kinase receptor in a Flt4-expressing cell, comprising contacting the cell with a polypeptide comprising:

a) amino acid residues 1 to 49 of SEQ ID NO:3;

b) amino acid residues 21 to 157 of SEQ ID NO:3;

c) amino acid residues 1 to 157 of SEQ ID NO:3;

d) amino acid residues 21 to 419 of SEQ ID NO:3; or

e) the amino acid sequence of SEQ ID NO:3,

in an amount effective to stimulate tyrosine phosphorylation of said Flt4 tyrosine kinase receptor.

59. (New) A method for promoting growth of endothelial cells that express Flt4 tyrosine receptor, comprising contacting the cells with a polypeptide comprising:

a) amino acid residues 1 to 49 of SEQ ID NO:3;

b) amino acid residues 21 to 157 of SEQ ID NO:3;

c) amino acid residues 1 to 157 of SEQ ID NO:3;

d) amino acid residues 21 to 419 of SEQ ID NO:3; or

e) the amino acid sequence of SEQ ID NO:3,

in an amount effective to promote the growth of the endothelial cells.